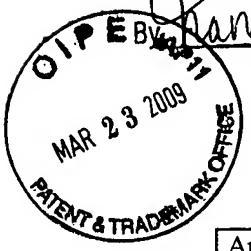
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.

By _____ Date 3/20/2009



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Nigel J. Liverton et al.		
Serial No.:	10/559,153	Case No.: 21414P	Group Art Unit: 1625
US Nat'l Filing Date:	December 5, 2005		
Int'l Appl'n No.:	PCT/US2004/017175		Examiner: Nizal S. Chandrukumar
Int'l Filing Date:	28 May 2004		
For:	3-FLUORO-PIPERIDINES AS NMDA/NR2B ANTAGONISTS		

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF RODNEY A. BEDNAR UNDER 37 C.F.R. § 1.132

I, Rodney A. Bednar, hereby declare as follows:

1. I am a citizen of the United States, and am over 21 years of age. I have been employed by Merck & Co., Inc., since 1991. I am presently Senior Investigator in Medicinal Chemistry at Merck. A copy of my curriculum vitae is attached at Exhibit A.

2. As part of my job responsibilities at Merck, during the period of from about 1999 to 2004, I was a member of Merck's NMDA/NR2B development team. One of my roles on the team was to provide biological testing of NMDA/NR2B ligands developed by Merck's medicinal chemists. The testing was done at my direction and under my supervision, in my laboratory at Merck's West Point, Pennsylvania research facility. The testing was done to evaluate the ligands as potential drug candidates. I tested compounds disclosed and claimed in both International Application WO 02/068409 and International Application WO 2004/108705.

3. I understand that the instant U.S. patent application for which I am making this Declaration is the U.S. national phase of the application published as WO 2004/108705.

4. The testing performed in my laboratory, and under my supervision, included *in vitro* binding assay studies of the NMDA/NR2B receptor.

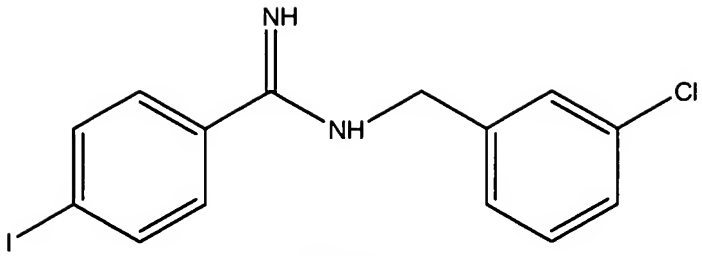
5. In Vitro Binding Assay. The radioligand binding assay was performed at room temperature in 96-well microtiter plates with a final assay volume of 1.0 mL in 20 mM Hepes buffer (pH 7.4) containing 150 mM NaCl. Solutions of NR2B antagonists were prepared in DMSO and serially diluted with DMSO to yield 20 μL of each of 10 solutions differing by 3-fold in concentration. Non-specific binding (NSB) was assessed using AMD-1 (10 μM final concentration), and total binding (TB) was measured by addition of DMSO (2% final concentration). Membranes expressing NR1a/NR2B receptors (40 pM final concentration) and tritiated AMD-2 (1 nM final concentration) were added to all wells of the microtiter plate. After 3 hours of incubation at room temperature, samples are filtered through Packard GF/B filters (presoaked in 0.05% PEI, polyethyleninine Sigma P-3143) and washed 10 times with 1 mL of cold 20 mM Hepes buffer per wash. After vacuum drying of the filter plates, 40 μL of Packard Microscint-20 was added and bound radioactivity determined in a Packard TopCount. The apparent dissociation constant (K_I), the maximum percentage inhibition ($\%I_{max}$), the minimum percentage inhibition ($\%I_{min}$) and the hill slope (nH) were determined by a non-linear least squares fitting the bound radioactivity (CPM bound) to Equation #2 below.

Equation #2:

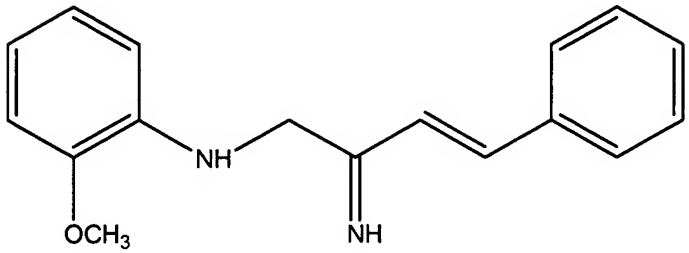
$$\text{CPM Bound} = \frac{(SB)\,(\%I_{max} - \%I_{min})\,/100}{(1 + ([Drug]/(K_I\,(1 + [AMD\text{-}2]/K_D)\,)\,)^{nH}\,)} + NSB + (SB)(100 - \%I_{max})/100$$

where, K_D is the apparent dissociation constant for the radioligand for the receptor as determined by a hot saturation experiment and SB is the specifically bound radioactivity determined from the difference of TB and NSB control wells.

AMD-1 and AMD-2 are shown below:



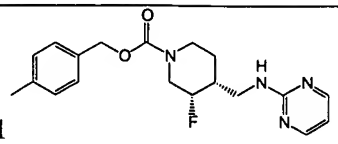
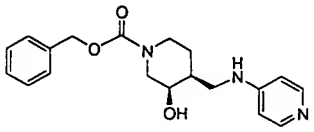
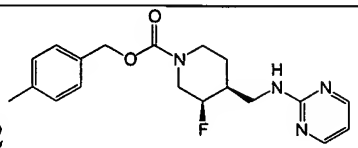
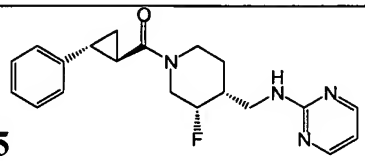
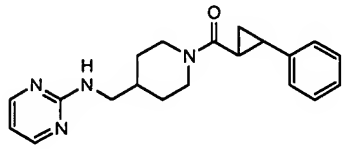
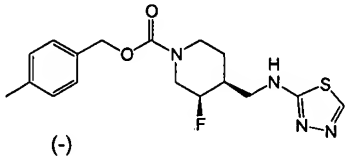
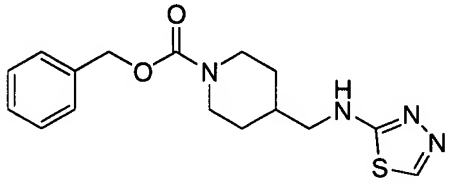
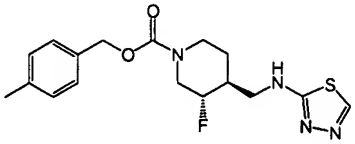
AMD-1



AMD-2

Ki values of representative compounds from the instant application and from WO 02/068409, are provided below in Table 1.

Table 1

Application Serial No. 10/559,153		WO 02/068409	
Example	Ki (nM)	Example	Ki (nM)
1 	4.7	**39** 	72
2 	22	**40** Separated Enantiomers of Example 39	56 and 70
5 	13	**171** 	32
6  (-)	41	**8** 	192
7 	28		

6. I further declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the instant application or any patent issued thereon.

Rodney A. Bednar

Dated:

CURRICULUM VITAE

I. PERSONAL

A. Name: **Dr. Rodney A. Bednar**

B. Home Address: 213 Musket Circle
Lansdale, PA 19446

C. Home Telephone Number: (215) 361-9349

II. EDUCATION

School	*Dates*	*Major*	*Degree*
Juniata College, Huntingdon, PA *summa cum laude* First in graduation class	1973 - 1977	Chemistry	B.S.
University of Delaware	1977 - 1982	Chemistry	Ph.D.
Brandeis University NIH Postdoctoral Fellow with Professor William P. Jencks	1982 - 1985	Biochemistry	

III. MRL EMPLOYMENT HISTORY

Title	*From - To*
Senior Investigator Department of Medicinal Chemistry April 2007- Department of Pain Research 2006-2007 Merck Research Laboratories	2005 - Present
Senior Research Fellow Department of Molecular Pharmacology Merck Research Laboratories	1998 - 2005
Research Fellow Biological Chemistry Dec 1991 - Nov 1993 Pharmacology Nov 1993 - 1998 Merck Research Laboratories	1991 - 1998

IV. NON-MRL EMPLOYMENT HISTORY

Title	*From - To*
Adjunct Associate Professor of Pharmacological Sciences School of Medicine SUNY at Stony Brook	1991 - Present
Associate Professor of Pharmacological Sciences School of Medicine SUNY at Stony Brook	1991

Assistant Professor of Chemistry 1986 - 1991
School of Arts & Sciences
SUNY at Stony Brook

Assistant Professor of Pharmacological Sciences 1985 - 1991
School of Medicine
SUNY at Stony Brook

V. ACADEMIC EXPERIENCE

See IV.

VI. TRAINING

Source	Date	Type	Certification
Introduction to Laboratory Automation Technology	20 Oct 2002	ISLAR Short Course	Yes
Introduction to Receptor Pharmacology	11 Sept 2004	SBS Short Course	Yes
Setting up a robust robotic and automated system for compound management	22 May 2005	IQPC Workshop	No
LIMS in the Organization	22 Jan 2006	ALA Short Course	Yes
Materials Management QC/QA Principles for Benchmark HTS	25 Sept 2006	IQPC Workshop	No

Effective Compound Library Storage and Distribution	25 Sept 2006	IQPC Workshop	No
Creating an Affordable, Expandable Solution for your Chemical Compound Storage Needs	25 Sept 2006	IQPC Workshop	No
The Communications Workshop (Leadership Effectiveness Training)	1-3 Nov 2006	Gordon Training	Yes
Methods in Drug Discovery: Fluorescence Assay in Drug Discovery	23-24 April 2007	Select Bioscience	Yes
Methods in Drug Discovery: Enzyme and Binding Assays in Drug Discovery	24-25 April 2007	Select Bioscience	Yes
Automated Molecular Assays for Drug Discovery: A Toolbox Approach to Selecting an Appropriate Assay Technology	April 2007	SBS Short Course	Yes
Career Coaching for Mangers	June 2007	Merck	No

VII. SOCIETY MEMBERSHIPS

Archives of Biochemistry and Biophysics, Editorial Board, 1995-2001
American Society for Biochemistry and Molecular Biology
Sigma Xi, The Scientific Research Society
American Chemical Society, Divisions of Biological and Medicinal Chemistry
American Heart Association Thrombosis Council
Society of Biomolecular Sciences 2004-2007
The Association of Laboratory Automation 2006-2007

VIII. ACADEMIC AND PROFESSIONAL HONORS

National Institutes of Health, "Chalcone Isomerase: Mechanism of Catalysis", 9/1/85-8/31/92.

National Institutes of Health Postdoctoral Fellowship, 1982 - 1985.

American Cancer Society Postdoctoral Fellowship. (Awarded but declined.)

Joel L. Silver Memorial Award, "in recognition of high achievement in original research". University of Delaware, 1980.

Glenn S. Skinner Memorial Award, "in recognition of high achievement in scholarship, research, and outstanding service to the Department of Chemistry", University of Delaware, 1980.

Department of Chemistry Fellowship, University of Delaware, 1979 - 1980.

Departmental "Excellence-In-Teaching Award", University of Delaware, 1978.

Unidel Fellow in Chemistry, University of Delaware, 1977 - 1981.

National Science Foundation Graduate Fellowship-Honorable Mention, 1977.

IX. PUBLICATIONS

1. C. R. Bacon, R. A. Bednar and R. F. Colman (1981) "The Reaction of 4-Iodoacetamindosalicyclic Acid with TPN-dependent Isocitrate Dehydrogenase from Pig Heart", *J. Biol. Chem.* **256**, 6593-6599.

2. K. V. Saradambal, R. A. Bednar, and R. F. Colman (1981) "Lysine and Tyrosine in the NADH Inhibitory Site of Bovine Liver Glutamate Dehydrogenase", *J. Biol. Chem.* **256**, 11866-11872.

3. R. A. Bednar, F. C. Hartman, and R. F. Colman (1982) "3-Bromo-2-ketoglutarate: A Substrate and Affinity Label for Diphosphopyridine Nucleotide Dependent Isocitrate Dehydrogenase", *Biochemistry* **21**, 3681-3689.

4. R. A. Bednar, F. C. Hartman, and R. F. Colman (1982) "3,4-Didehydro-2-ketoglutarate: An Affinity Label for Diphosphopyridine Nucleotide Dependent Isocitrate Dehydrogenase", *Biochemistry* **21**, 3689-3697.

5. R. A. Bednar and R. F. Colman (1982) "Chemical Modification: A Probe of the Structure and Function of the Subunits and DPN-Dependent Isocitrate Dehydrogenase", *J. Biol. Chem.* **257**, 11734-11739.

6. R. A. Bednar and R. F. Colman (1982) "Synthesis, Characterization, and Reactions of 2'-, 3'-, and 5'-(2-Bromoethyl)-AMP: Potential Affinity Labels for Nucleotide Binding Sites in Enzymes.", J. Prot. Chem. 1, 203-224.

7. R. A. Bednar and W. P. Jencks (1985) "Is HCN a Normal Acid? Proton Transfer from HCN to Bases and Small Inhibition of Proton Exchange of Acids", *J. Am. Chem. Soc.* **107**, 7117-7125.

8. R. A. Bednar and W. P. Jencks (1985) "Direct Proton Transfer Between HCN and Amines", *J. Am. Chem. Soc.* **107**, 7126-7134.

9. R. A. Bednar and W. P. Jencks (1985) "Intramolecular Proton Transfer through Water in Diamines", *J. Am. Chem. Soc.* **107**, 7135-7138.

10. R. A. Bednar and J. R. Hadcock (1988) "Purification and Characterization of Chalcone Isomerase from Soybeans", *J. Biol. Chem.* **263**, 9582-9588.

11. R. A. Bednar, W. B. Fried, Y. W. Lock and B. Pramanik (1989) "Chemical Modification of Chalcone Isomerase by Mercurials and Tetrathionate: Evidence for a Single Cysteine in the Active Site", *J. Biol. Chem.* **264**, 14272-14276.

12. R. A. Bednar (1990) "Reactivity and pH Dependence of Thiol Conjugation to N-Ethylmaleimide: Detection of a Conformational Change in Chalcone Isomerase", *Biochemistry* **29**, 3684-3690.

13. R. A. Bednar and A. J. Adeniran (1990) "Chemical Modification of Chalcone Isomerase by Diethyl Pyrocarbonate: Histidine Residues are not Essential for Catalysis", *Arch. Biochem. Biophys.* **282**, 393-398.

14. R. A. Bednar, C. McCaffrey, and K. Shan (1991) "Introduction of Unnatural Amino Acids into Chalcone Isomerase", *Bioconj. Chem.* **2**, 211-216.

15. C. Y. Hsu, P. E. Persons, A. P. Spada, R. A. Bednar, A. Levitzki, and A. Zilberstein (1991) "Kinetic Analysis of the Inhibition of Epidermal Growth Factor Receptor Tyrosine Kinase by Lavendustin-A and Its Analogue", *J. Biol. Chem.* **266**, 21105-21112.

16. L. Waxman, K. P. Doshi, S. L. Gaul, S. P. Wang, R. A. Bednar and A. M. Stern (1994) "Identification and Characterization of Endothelin-Converting Activity from EAHY-926 Cells: Evidence for the Physiologically Relevant Human Enzyme", *Arch. Biochem. Biophysics.* **308**, 240-253.

17. M. S. Egbertson, B. Bednar, R. A. Bednar, G. D. Hartman, R. J. Gould, R. J. Lynch, L. M. Vassallo, S. D. Young (1996) "Nonpeptide Glycoprotein IIb/IIIa Inhibitors. 9. Centrally Constrained Alpha-Sulfonamides Are Useful Tools For Exploring Platelet Receptor Function", *Biorganic & Medicinal Chemistry Letters*, **6**, 1415-1420.

18. M. S. Egbertson, G. D. Hartman, R. J. Gould, B. Bednar, R. A. Bednar, J. J. Cook, S. L. Gaul, M. A. Holahan, L. A. Libby, J. J. Lynch, G. R. Sitko, M. T. Stranieri, L. M.

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19. J. D. Prugh, R. J. Gould, R. J. Lynch, G. Zhang, J. J. Cook, M. A. Holahan, M. T. Stranieri, G. R. Sitko, S. L. Gaul, R. A. Bednar, B. Bednar, G. D. Hartman (1997) "Nonpeptide GP IIb/IIIa Inhibitors. 16. Thieno[2,3-b]Thiophene Alpha-Sulfonamides Are Potent Inhibitors of Platelet Aggregation", *Biorganic & Medicinal Chemistry Letters*, **7**, 865-870.

20. B. C. Askew, R. A. Bednar, B. Bednar, D. A. Claremon, J. J. Cook, C. J. McIntyre, C.A. Hunt, R. J. Gould, R. J. Lynch, J. J. Lynch, S. L. Gaul, M. T. Stranieri, G. R. Sitko, M. A. Holahan, J. D. Glass, T. Hamill, L. M. Gorham, T. Prueksaritanont, J. J. Baldwin, and G. D. Hartman (1997) "Non-Peptide Glycoprotein IIb/IIIa Inhibitors. 17. Design and Synthesis of Orally Active, Long-Acting Non-Peptide Fibrinogen Receptor Antagonists", *J. Med. Chem.* **40**, 1779-1788.

21. B. Bednar, M. E. Cunningham, P. A. McQueney, M. S. Egbertson, B. C. Askew, R. A. Bednar, G. D. Hartman, and R. J. Gould (1997) "Flow Cytometric Measurement of Kinetics and Equilibrium Binding Parameters of Arginine-Glycine-Aspartic Acid Ligands in Binding to Glycoprotein IIb/IIIa on Platelets", *Cytometry* **28**, 58-65.

22. D. G. Abraham, E. M. Nutt, R. A. Bednar, B. Bednar, R. J. Gould, and L. T. Duong (1997) "Arginine Glycine Aspartic Acid Mimics can Indentify Transitional Activation State of Recombinant $\alpha_{IIb}\beta_3$ in Human Embryonic Kidney 293 Cells", *Molecular Phamacology,* **52**, 227-236.

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27. M. S. Egbertson, B. Bednar, B. C. Askew, R. A. Bednar, K. Brashear, M. J. Breslin, M. E. Duggan, T. E. Fisher, W. Halczenko, J. H. Hutchinson, N. Ihle, J. D. Prugh, J. S. Wai, R. J. Gould, G. D. Hartman (2000) "Non-Peptide GP IIb/IIIa Inhibitors. Part 21: C-6 Flexibility and Amide Bond Orientation are Important Factors in Determining the Affinity of Compounds for Activated and Resting Platelet Receptors.", *Biorganic & Medicinal Chemistry Letters* **10**, 1943-1948.

28. J. C. Barrow, P.G. Nantermet, H. G. Selnick, K. L. Glass, P. L. Ngo, M. B. Young, J. M. Pellicore, M. J. Breslin, J. H. Hutchinson, R. M. Freidinger, C. Condra, J. Karczewski, R. A. Bednar, S. L. Gaul, A. Stern, R. Gould, T. M. Connolly (2001) "Discovery and Initial Structure-Activity Relationships of Trisubstituted Ureas as Thrombin Receptor (PAR-1) Antagonists", *Biorganic & Medicinal Chemistry Letters* **11**, 2691-2696.

29. P.G. Nantermet, J. C. Barrow, G. F. Lundel, J. M. Pellicore, K.E. Rittle, M. B. Young, R. M. Freidinger, T. M. Connolly, C. Condra, J. Karczewski, R. A. Bednar, S. L. Gaul, R. J. Gould, K. Prendergast, H. G. Selnick (2002) "Discovery of a Nonpeptidic Small Molecule Antagonist of the Human Platelet Thrombin Receptor (PAR-1)", *Biorganic & Medicinal Chemistry Letters* **12**, 319-323.

30. C. F. Claiborne, J. A. McCauley, B. E. Libby, N. R. Curtis, H. J. Diggle, J. J. Kulagowski, S. R. Michelson, K. D. Anderson, D. A. Claremon, R. M. Freidinger, R. A. Bednar, S. D. Mosser, S. L. Gaul, T. M. Connolly, C. L. Condra, B. Bednar, G. L. Stump, J. J. Lynch, A. Macaulay, K. A. Wafford. K. S. Koblan, N. J. Liverton (2003) "20. Orally efficacious NR2B-selective NMDA receptor antagonists", Biorganic & Medicinal Chemistry Letters 13, 679-700.

31. S. D. Mosser, S. L. Gaul, B. Bednar, K. S. Koblan, and R. A. Bednar (2003) "Automation of In Vitro Dose-Inhibition Assays Utilizing the Tecan Genesis and an Integrated Software Package to Support the Drug Discovery Process", *J. of the Association for Laboratory Automation*, **8**, 54-63.

32. J. A. McCauley, C. R. Theberge, J. J. Romano, S. B. Billings, K. D. Anderson, D. A. Claremon, R. M. Freidinger, R. A. Bednar, S. D. Mosser, S. L. Gaul, T. M. Connolly, C. L. Condra, M. H. Xia, M. E. Cunningham, B. Bednar, G. L. Stump, J. J. Lynch, A. Macaulay, K. A. Wafford, K. S. Koblan, N. J. Liverton (2004) "NR2B-selective N-methyl-D-aspartate antagonists: Synthesis and evaluation of 5-substituted benzimidazoles", *J. Med. Chem.* **47**, 2089-2096.

33. Kiss, Laszlo; Cheng, Gong; Bednar, Bohumil; Bednar, Rodney A.; Bennett, Paul B.; Kane, Stefanie A.; McIntyre, Charles J.; McCauley, John A.; Koblan, Kenneth S. **In vitro characterization of novel NR2B selective NMDA receptor antagonists.** Neurochemistry International (2005), 46(6), 453-464.

34. Bell, Ian M.; Bednar, Rodney A.; Fay, John F.; Gallicchio, Steven N.; Hochman, Jerome H.; McMasters, Daniel R.; Miller-Stein, Cynthia; Moore, Eric L.; Mosser, Scott D.; Pudvah, Nicole T.; Quigley, Amy G.; Salvatore, Christopher A.; Stump, Craig A.; Theberge, Cory R.; Wong, Bradley K.; Zartman, C. Blair; Zhang, Xu-Fang; Kane,

Stefanie A.; Graham, Samuel L.; Vacca, Joseph P.; Williams, Theresa M. **Identification of novel, orally bioavailable spirohydantoin CGRP receptor antagonists.** Bioorganic & Medicinal Chemistry Letters (2006), 16(24), 6165-6169.

35. Liverton, Nigel J.; Bednar, Rodney A.; Bednar, Bohumil; Butcher, John W.; Claiborne, Christopher F.; Claremon, David A.; Cunningham, Michael; DiLella, Anthony G.; Gaul, Stanley L.; Libby, Brian E.; Lyle, Elizabeth A.; Lynch, Joseph J.; McCauley, John A.; Mosser, Scott D.; Nguyen, Kevin T.; Stump, Gary L.; Sun, Hong; Wang, Hao; Yergey, James; Koblan, Kenneth S. **Identification and Characterization of 4-Methylbenzyl 4-[(Pyrimidin-2-ylamino)methyl]piperidine-1-carboxylate, an Orally Bioavailable, Brain Penetrant NR2B Selective N-Methyl-D-Aspartate Receptor Antagonist.** Journal of Medicinal Chemistry (2007), 50(4), 807-819

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Published Abstracts on Merck Research

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18. Mosser,-S-D; Fay,-J-F; Lemaire,-W; Harkins,-T; Williams,-E; Koblan,-K-S; Kane, -S-A; Bednar,-R-A. The Evolution of the Lead Optimization Phase of Drug Discovery. Drug Discovery Technology Symposium, Boston, MASS. 2006 Aug 7.

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21. KEMMERER, A., MOSSER, S.D., LEMAIRE, W., DESAI, R.R., DELLA PENNA, K.B., KOBLAN, K.S., KANE, S.A., BEDNAR, R.A. Overcoming the challenges of minimizing dead volume requirements in assay automation for lead optimization. For presentation at: Society For Biomolecular Sciences 13th Annual Conference And Exhibition, Montreal, Canada, 4/15/07 - 4/19/07.

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23. FAY, J.F., WILLIAMS, E.A., MOSSER, S.D., HARRELL, C.M., CALAMARI, A., MULLEN, F.A., HARKINS, T., BEDNAR, R.A. Automation of nanoliter volume transfers: doing more with less. For presentation at: Drug Discovery And Development Of Innovative Therapeutics 12th Annual World Congress (ddt), Boston, Massachusetts, 8/6/07 - 8/9/07.

24. MOSSER, S.D., FAY, J.F., LEMAIRE, W., HARKINS, T., WILLIAMS, E.A., KEMMERER, A., MULLEN, F.A., MARTIN, B., BRUNO, J.G., BARROW, J.C., BEDNAR, R.A. Supporting the lead optimization phase of drug discovery. For presentation at: Ttp Labtech Open Day, Royston, United Kingdom, 10/4/07 - 10/5/07.

Invited Lectures on Merck Research

August 11, 1997	Red Bank Symposium on VLA4 "Novel Mechanism for Long Acting GP IIb/IIIa Antagonists and Identification of Low Molecular Weight GP IIb/IIIa Antagonists that Bind Preferentially to Activated Platelets"
March 12&13, 2003	ADA Scientific Presentation: One Example of Best Practices at Merck.
Sept 26, 2006	"Automation & Workflow to Support the Lead Optimization Phase of Drug Discovery". 2nd Compound Management and QC Summitt
Oct 3, 2006	"FAST Assay Management for Lead Optimization". Automated Biotechnology and Global HTS Forum.
June 2007	Invited Speaker for Laboratory Robotics Interest Group Meeting

Internal Documents

1. S. D. Mosser, S. Lee Gaul, and R. A. Bednar (2002) "Operational Excellence in Biological Assays that Support Drug Discovery: Traditions Broken". West Point Novel Target & Technologies Session.

2. R. A. Bednar, S. Lee Gaul, S. D. Mosser (2002) "Artificial Intelligence in the Analysis of Dose Inhibition Profiles." West Point Novel Target & Technologies Session.

3. MRL Nonclinical Report: In Vitro and In Vivo Pharmacological Studies with L-001067743: An NMDA-NR2B Receptor Antagonist. Report L-001067743-85145-1. 19-July-2004.

4. R. A. Bednar (2004). "FAST: Facility for Assay and Screening Technology".